App's

L4 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1998:197516 CAPLUS Full-text
DN 128:270870
TI Preparation of 3-mercaptoacetylamino-1,5-substituted-2-azepinone derivatives as matrix metalloproteinase inhibitors
IN Warshawsky, Alan M.; Flynn, Gary A.; Patel, Meena V.; Beight, Douglas W.; Burkhart, Joseph P.; Tsay, Jiu-Tsair; Janusz, Michael J.; Shen, Jian; Dharanipragada, Ramalinga M.
PA Hoechst Marion Roussel, Inc., USA
SO PCT Int. Appl., 160 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9812211	A1	19980326	WO 1997-US13738	19970804
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	AU 9738278	A1	19980414	AU 1997-38278	19970804
	AU 718055	B2	20000406		
	EP 928291	A1	19990714	EP 1997-935308	19970804
	EP 928291	B1	20021204		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	CN 1234039	A	19991103	CN 1997-199024	19970804
	BR 9713207	A	20000404	BR 1997-13207	19970804
	NZ 334490	A	20000825	NZ 1997-334490	19970804
	JP 2001501926	T2	20010213	JP 1998-514658	19970804
	AT 229034	E	20021215	AT 1997-935308	19970804
	PT 928291	T	20030331	PT 1997-97935308	19970804
	ES 2184126	T3	20030401	ES 1997-935308	19970804
	TW 445262	B	20010711	TW 1997-86113339	19970913
	ZA 9708307	A	19980319	ZA 1997-8307	19970915
	MX 9902577	A	20000131	MX 1999-2577	19990317
	NO 9901316	A	19990518	NO 1999-1316	19990318
	HK 1020741	A1	20030502	HK 1999-105993	19991221
PRAI	US 1996-719291	A	19960919		
	WO 1997-US13738	W	19970804		

OS MARPAT 128:270870
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The present invention relates to certain novel title compds. I [R1 = C1-6 alkyl, W-(CH2)m, Q-Z-(CH2)m; W = phthalimido; Z = bond, O, NR6, CONR6, NR6CO, NHCONR6, O2CNR6, NHCO2, SO2NR6; Q = H, Y-(CH2)n; Y = H, C6-10 aryl, C3-9 heteroaryl, CO2R6, NR62, morpholino, piperidino, pyrrolidino, isoindolyl; R2 = C1-4 alkyl, (CH2)p-(C3-9) heteroaryl, (CH2)p-Ar1; Ar1 = (un)substituted Ph or naphthyl; R3 = H, C1-6 alkyl, CH2SCH2NHAc, (CH2)p-A, (CH2)m-B, CH2-D-R7; A = C6-10 aryl, C3-9 heteroaryl, cyclohexyl; B =

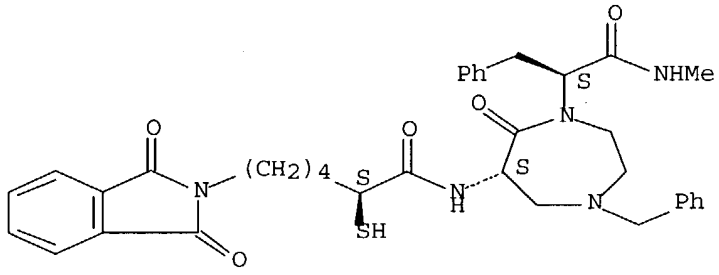
NR72, guanidino, nitroguanidino, CO2R6, CONR6; D = O, S; R4 = H, (CH2)m-S(O)pX1(R6)2; R5 = H, C1-6 alkyl; NR4R5 = piperidino, pyrrolidino, isoindolyl; R6 = H, C1-6 alkyl; R7 = H, C1-4 alkyl, (CH2)p-Ar1; R8 = H, CO2R7, CO(CH2)q-K, S-G; K = nitrogen-containing heterocycle, NR9R10; G = substituted alkyl; R9, R10 = independently C1-4 alkyl, (CH2)p-Ar1; X, X1 = independently CH, N; m = 2-4; n = 0-4; p = 0-2; q = 0-5] as matrix metalloproteinase inhibitors. Pharmaceutical compns. containing said compds. as well as methods of treating various disease states responding to inhibition of matrix metalloproteinase are also claimed herein. Thus, reductive alkylation of H-L-Phe-NHMe.HCl with azido aldehyde II (prepared in 5 steps from 4-phenylcyclohexanone), followed by deesterification and cyclization gave cis azepine III and its corresponding trans isomer in a 4:5 ratio. Reduction of III with 1,3-propanedithiol gave the corresponding amine, which was coupled with 2-bromo-6-phthalimidohexanoic acid to give bromide IV (R = Br). Substitution of IV (R = Br) with p-methoxybenzyl mercaptan followed by deprotection gave title compound IV (R = SH) (MDL 108,180). MDL 108,180 inhibited matrix metalloproteinases MMP-2, MMP-3, and MMP-12 in vitro with Ki = 1.2 nM, 39 nM, and 18 nM, resp.

IT **205391-09-9P 205391-10-2P 205391-11-3P**
205391-12-4P 205391-13-5P 205496-75-9P, MDL 108180 **205496-76-0P**, MDL 106540
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (preparation of substituted (mercaptoacetylamino)azepinone derivs. as matrix metalloproteinase inhibitors)

RN 205391-09-9 CAPLUS

CN 2H-Isoindole-2-hexanamide, N-[hexahydro-1-[2-(methylamino)-2-oxo-1-(phenylmethyl)ethyl]-7-oxo-4-(phenylmethyl)-1H-1,4-diazepin-6-yl]-1,3-dihydro-α-mercapto-1,3-dioxo-, [6S-[1(R*),6R*(R*)]]- (9CI) (CA INDEX NAME)

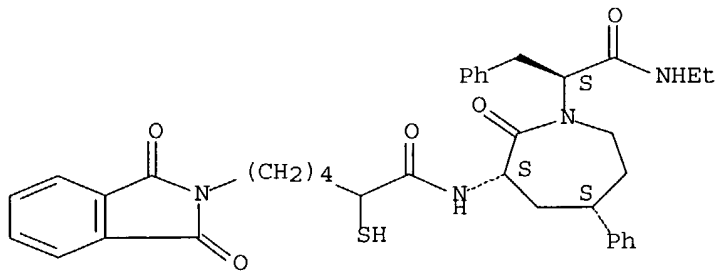
Absolute stereochemistry.



RN 205391-10-2 CAPLUS

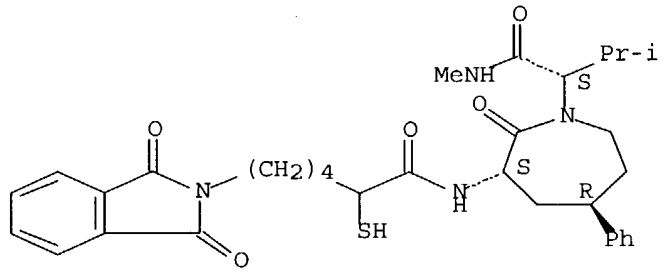
CN 2H-Isoindole-2-hexanamide, N-[1-[2-(ethylamino)-2-oxo-1-(phenylmethyl)ethyl]hexahydro-2-oxo-5-phenyl-1H-azepin-3-yl]-1,3-dihydro-α-mercapto-1,3-dioxo-, [3S-[1(R*),3α,5α]]-[partial]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



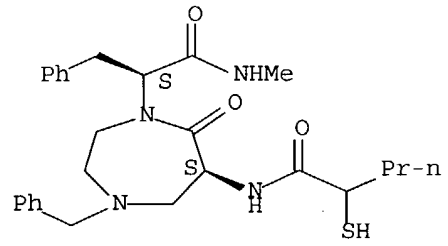
RN 205391-11-3 CAPLUS
CN 2H-Isoindole-2-hexanamide, N-[hexahydro-1-[2-methyl-1-[(methylamino)carbonyl]propyl]-2-oxo-5-phenyl-1H-azepin-3-yl]-1,3-dihydro-α-mercapto-1,3-dioxo-, [3S-[1(R*),3α,5β]]-[partial]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



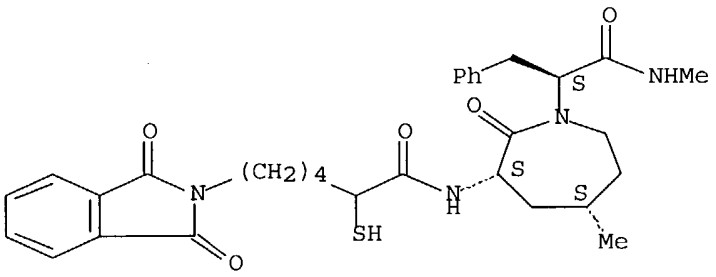
RN 205391-12-4 CAPLUS
CN 1H-1,4-Diazepine-1-acetamide, hexahydro-6-[(2-mercapto-1-oxopentyl)amino]-N-methyl-7-oxo-α,4-bis(phenylmethyl)-, [6S-[1(R*),6R*]]-[partial]-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



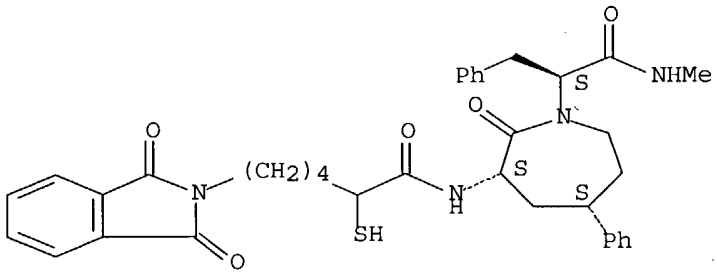
RN 205391-13-5 CAPLUS
CN 2H-Isoindole-2-hexanamide, N-[hexahydro-5-methyl-1-[2-(methylamino)-2-oxo-1-(phenylmethyl)ethyl]-2-oxo-1H-azepin-3-yl]-1,3-dihydro-α-mercapto-1,3-dioxo-, [3S-[1(R*),3α,5α]]-[partial]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



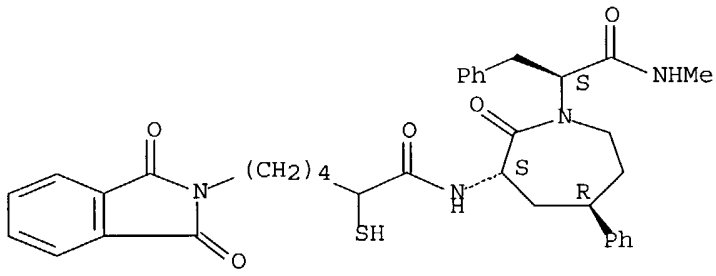
RN 205496-75-9 CAPLUS
CN 2H-Isoindole-2-hexanamide, N-[(3S,5S)-hexahydro-1-[(1S)-2-(methylamino)-2-oxo-1-(phenylmethyl)ethyl]-2-oxo-5-phenyl-1H-azepin-3-yl]-1,3-dihydro-α-mercapto-1,3-dioxo- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



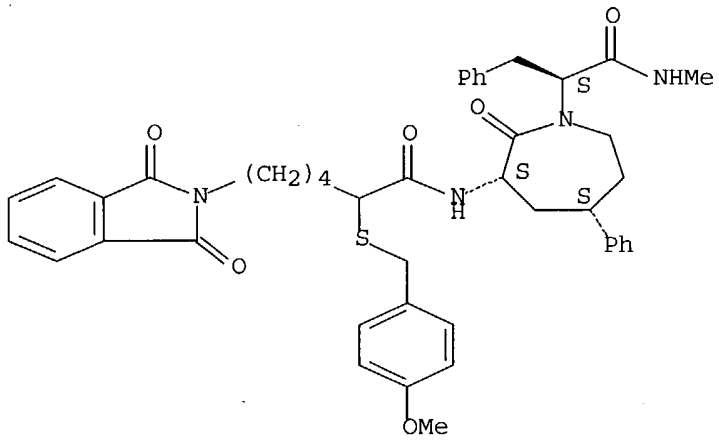
RN 205496-76-0 CAPLUS
CN 2H-Isoindole-2-hexanamide, N-[(3S,5R)-hexahydro-1-[(1S)-2-(methylamino)-2-oxo-1-(phenylmethyl)ethyl]-2-oxo-5-phenyl-1H-azepin-3-yl]-1,3-dihydro-α-mercapto-1,3-dioxo- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **205391-25-9P 205391-28-2P 205391-41-9P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)(preparation of substituted (mercaptoacetylamino)azepinone derivs. as matrix metalloproteinase inhibitors)
RN 205391-25-9 CAPLUS
CN 2H-Isoindole-2-hexanamide, N-[hexahydro-1-[2-(methylamino)-2-oxo-1-(phenylmethyl)ethyl]-2-oxo-5-phenyl-1H-azepin-3-yl]-1,3-dihydro-α-[[(4-methoxyphenyl)methyl]thio]-1,3-dioxo-, [3S-[1(R*),3α,5α]]-[partial]- (9CI) (CA INDEX NAME)

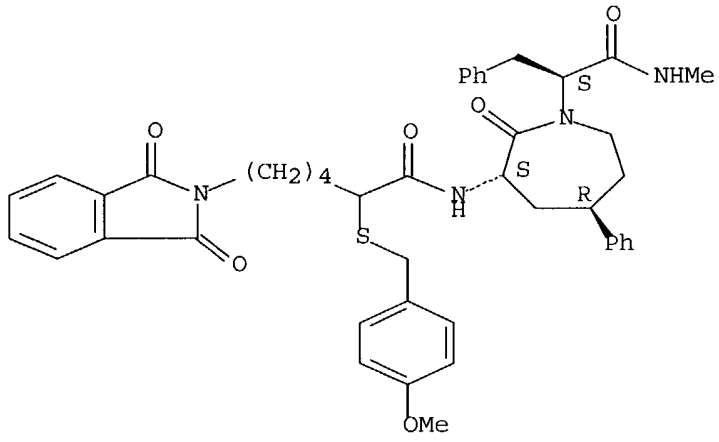
Absolute stereochemistry.



RN 205391-28-2 CAPLUS

CN 2H-Isoindole-2-hexanamide, N-[hexahydro-1-[2-(methylamino)-2-oxo-1-(phenylmethyl)ethyl]-2-oxo-5-phenyl-1H-azepin-3-yl]-1,3-dihydro-α-[[(4-methoxyphenyl)methyl]thio]-1,3-dioxo-, [3S-[1(R*),3α,5β]]-[partial]- (9CI) (CA INDEX NAME)

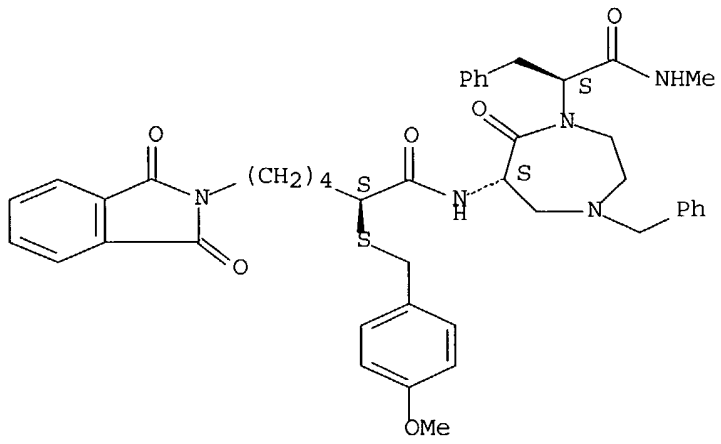
Absolute stereochemistry.



RN 205391-41-9 CAPLUS

CN 2H-Isoindole-2-hexanamide, N-[hexahydro-1-[2-(methylamino)-2-oxo-1-(phenylmethyl)ethyl]-7-oxo-4-(phenylmethyl)-1H-1,4-diazepin-6-yl]-1,3-dihydro-α-[[(4-methoxyphenyl)methyl]thio]-1,3-dioxo-, [6S-[1(R*),6R*(R*)]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 1 OF 8 MARPAT COPYRIGHT 2004 ACS on STN
AN 139:338195 MARPAT Full-text
TI Preparation of peptides as inhibitors of serine proteases, particularly HCV NS3-NS4A protease
IN Pitlik, Janos; Cottrell, Kevin M.; Farmer, Luc J.; Perni, Robert B.; Courtney, Lawrence F.; Van Drie, John H.; Murcko, Mark A.
PA Vertex Pharmaceuticals, Inc., USA
SO PCT Int. Appl., 210 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

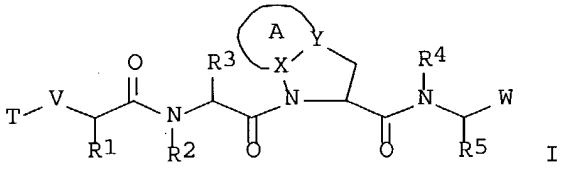
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2003087092	A2	20031023	WO 2003-US11459	20030411

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2004018986	A1	20040129	US 2003-412600	20030411

PRAI US 2002-371846P 20020411
GI



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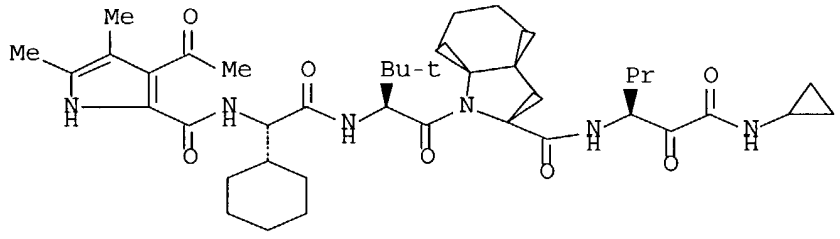
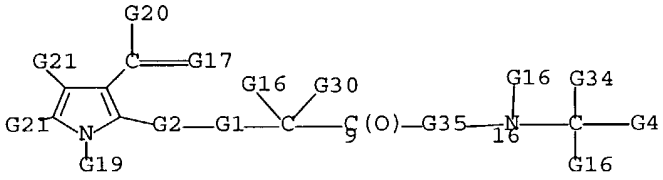


II

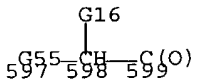
AB The invention relates to compds. I [A together with X and Y is a 3- to 6-membered aromatic or non-aromatic ring having up to 3 heteroatoms; R1, R3 are aliphatic, (un)substituted (cyclo)alk(en)yl, (hetero)aryl, etc.; R2, R4 are H, (un)substituted aliphatic, cycloalkyl or aryl aliphatic; R5 is (un)substituted aliphatic; W is COCOR6, COCO2R6, or COCONR62, where R6 is H, aliphatic, (hetero)aryl, etc.; V is CONR8, SONR8, SO2NR8, where R8 is H or aliphatic; T is (hetero)aryl, aliphatic,

sulfonylaminoalkyl, etc.] that inhibit serine protease activity, particularly the activity of hepatitis C virus NS3-NS4A protease. Thus, peptide II was prepared via coupling reactions in solution and showed Ki and IC50 values < 0.5 μM.

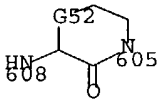
MSTR 2



G1 = S
G35 = 597-9 599-16



G52 = (0-2) CH2
G55 = 608-9 605-598

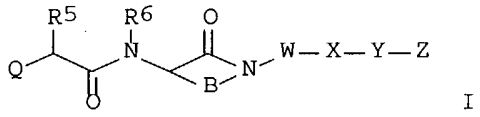


MPL: claim 26
NTE: additional derivatization also claimed

L9 ANSWER 2 OF 8 MARPAT COPYRIGHT 2004 ACS on STN
AN 135:303916 MARPAT Full-text
TI Preparation of substituted lactams as inhibitors of aβ protein production
IN Han, Wei; Liu, Hong; Olson, Richard E.; Yang, Michael G.
PA DuPont Pharmaceuticals Company, USA
SO PCT Int. Appl., 201 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001077086	A1	20011018	WO 2001-US11714	20010411
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	US 2002025955	A1	20020228	US 2001-832455	20010411
	US 6632812	B2	20031014		
	EP 1289966	A1	20030312	EP 2001-930471	20010411
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
	JP 2004500419	T2	20040108	JP 2001-575561	20010411
PRAI	US 2000-196549P	20000411			
	WO 2001-US11714	20010411			

GI



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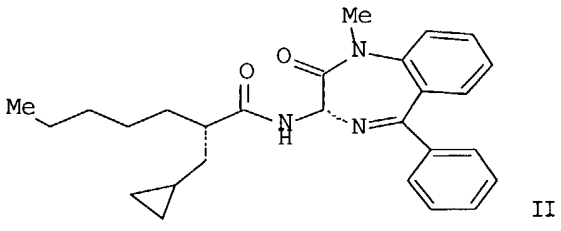
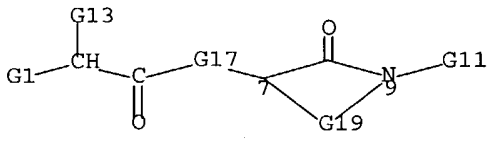


II

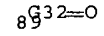
AB The title compds. I [wherein Q = (CR7R7a)mR4, (CR7R7a)nSR4, (CR7R7a)nOR4, (CR7R7a)mN(R7b)R4, (CR7R7a)nSOR4, (CR7R7a)nSO2R4, or (CR7R7a)nCOR4, provided when n = 0, then R4 ≠ H; m = 1-3; n = 0-2; R4,

R5, and Z = independently H or (un)substituted alkyl, alkenyl, alkynyl, carbocycle, aryl, or heterocycle; R6 = H or (un)substituted alkyl, carbocycle, or aryl; R7 and R7a = independently H or alkyl; R7b = H or alkyl; ring B = (un)substituted 7-membered lactam; W = a bond or (CR8R8a)p; p = 0-4; R8 and R8a = independently H, F, (cyclo)alkyl, alkenyl, or alkynyl; X = a bond or (un)substituted aryl, carbocycle, or heterocycle; Y = a bond or (CR9R9a)tV(CR9R9a)u; t and u = independently 0-2; R9 and R9a = independently H, F, or (cyclo)alkyl; V = a bond, CO, O, S, SO, SO2, or (un)substituted amino, carbamoyl, carbonylamino, sulfamoyl, aminosulfonyl, carboxy, etc.] were prepared For example, coupling of (3S)-3-amino-1,3- dihydro-1-methyl-5-phenyl-2H-1,4-benzodiazepin-2-one with (αR)-α-[(1S)-1-hydroxypentyl]cyclopropanepropanoic acid (58%), followed by reaction with thiocarbonyldiimidazole (71%) and reduction with Bu3SnH (85%), gave II. I inhibit the processing of amyloid precursor protein and, more specifically, inhibit the production of Aβ-peptide, thereby acting to prevent the formation of neurol. deposits of amyloid protein (no data). Thus, I are useful for the treatment of neurol. disorders related to β-amyloid production, such as Alzheimer's disease and Down's Syndrome (no data).

MSTR 1



G9 = S
G17 = NH
G19 = CH2CH2CH2CH2 (SO)
G20 = Ak<EC (1-) C, BD (0-) D (0-) T> (SO G21)
G24 = 89



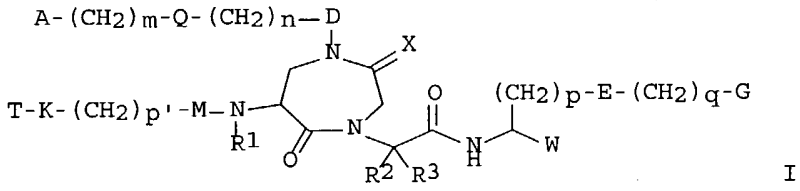
G31 = Hy<EC (5-10) A (1-4) Q (0-) O (0-) S (0-) N (0) OTHERQ> (SO)
G32 = Ak<EC (1-) C, BD (ALL) SE> (SO G21)
MPL: claim 1
NTE: or pharmaceutically acceptable salts or prodrugs
NTE: additional ring formation also claimed

RE.CNT 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 3 OF 8 MARPAT COPYRIGHT 2004 ACS on STN
AN 133:296661 MARPAT Full-text
TI Preparation of diazepine peptide derivatives as selective factor Xa inhibitors
IN Scarborough, Robert M.; Zhu, Bing-yan
PA Cor Therapeutics Inc, USA
SO U.S., 32 pp.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 6133256	A	20001017	US 1998-58566	19980413
	AU 746596	B2	20020502	AU 2000-55079	20000831
PRAI	US 1997-69323P		19970414		

GI



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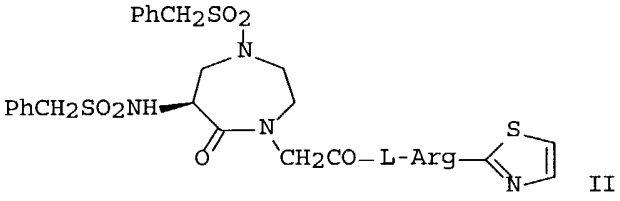
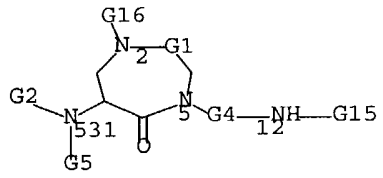


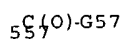
II

AB Novel compds. I [R1, R2 = H, alkyl, cycloalkyl, alkylaryl, alkylcycloalkyl, aryl; R3 = H or CR2R3 is a carbocyclic ring; m = 0-2; n = 0-6; p, p' = 0-4; q = 0-1; A, T, G = H, OH, alkyl, aryl, amino, guanidino, etc.; Q, K, E is a direct link, cycloalkyl, aryl, heterocyclyl containing 1-4 heteroatoms N, O, and S, etc.; D, M is a direct link, CO, SO2, O2C, NR9SO2, NR9CO, where R9 = H, OH, alkyl, aryl, or alkylaryl; X = O or H2; W = H, acyl, or borate group] were prepared as inhibitors of factor Xa. The compds. are useful in vitro or in vivo for preventing or treating coagulation disorders. Thus, diazepinone arginine derivative II was prepared by a multistep procedure involving cyclization of (S)- CbzNHCH(CO2CMe3)CH2NBnCH2CH2NBocCH2CO2Me (Cbz = benzyloxycarbonyl, Bn = benzyl, Boc = tert-butoxycarbonyl) to form the diazepinone ring system.

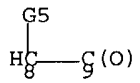
MSTR 1



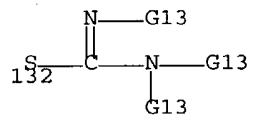
G1 = C(O)
G2 = 557



G4 = 8-5 9-12



G8 = Ak<EC (1-10) C, BD (0-) D (0) T>
G30 = 132



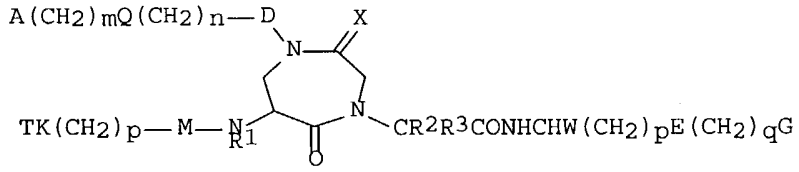
MPL: claim 1
NTE: and pharmaceutically acceptable salts
NTE: additional ring formation also claimed
NTE: substitution is restricted
STE: and optical isomers

RE.CNT 139 THERE ARE 139 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

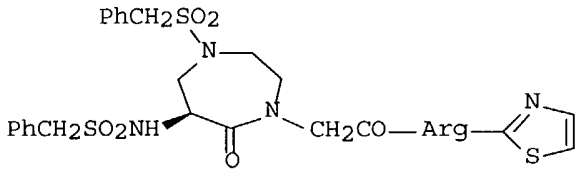
L9 ANSWER 4 OF 8 MARPAT COPYRIGHT 2004 ACS on STN
AN 129:331052 MARPAT Full-text
TI Preparation of selective factor Xa inhibitors
IN Scarborough, Robert M.; Zhu, Bing-yan
PA Cor Therapeutics, Inc., USA
SO PCT Int. Appl., 58 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9846628	A1	19981022	WO 1998-US7161	19980413
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT; BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	AU 9868964	A1	19981111	AU 1998-68964	19980413
	AU 741099	B2	20011122		
	EP 975659	A1	20000202	EP 1998-914659	19980413
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	NZ 500351	A	20011026	NZ 1998-500351	19980413
	JP 2001521524	T2	20011106	JP 1998-544069	19980413
	MX 9909137	A	20000228	MX 1999-9137	19991006
	AU 746596	B2	20020502	AU 2000-55079	20000831
PRAI	US 1997-69323P	19970414			
	WO 1998-US7161	19980413			

GI



I

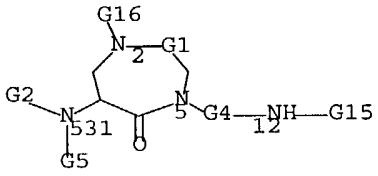


II

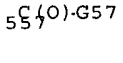
AB Heterocyclyl peptides I [R1, R2 = H, alkyl, cycloalkyl, alkylaryl, alkylcycloalkyl, aryl; R3 = H or R2 and R3 together form a carbocyclic

ring; m = 0-2; n = 0-6; p = 0-4; q = 0-1; A, T, G = H, OH, alkyl, aryl, alkylaryl, or various amine-containing groups; Q = null, alkyl, cycloalkyl, alkenyl, alkenylaryl, aryl, heterocyclyl; D, M = null, CO, SO2, OCO, (un)substituted iminosulfonyl or iminocarbonyl; X = O, H2; K = null, cycloalkyl, alkenyl, alkenylaryl, aryl, heterocyclyl; E = null, cycloalkyl, aryl, heterocyclyl; W = H, acyl, borate moiety] were prepared as factor Xa inhibitors. Compds. of the invention, e.g., II, have IC50 values <500 nM in the factor Xa assay.

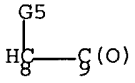
MSTR 1



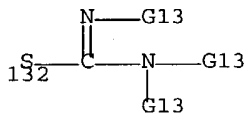
G1 = C(O)
G2 = 557



G4 = 8-5 9-12



G8 = Ak<EC (1-10) C, BD (0-) D (0) T>
G30 = 132



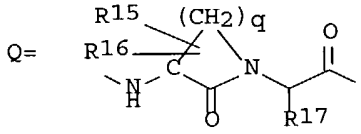
DER: and pharmaceutically acceptable salts
MPL: claim 1
NTE: additional ring formation also claimed
NTE: substitution is restricted
STE: and optical isomers

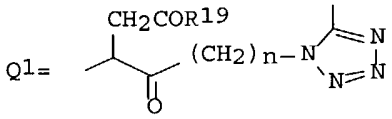
RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

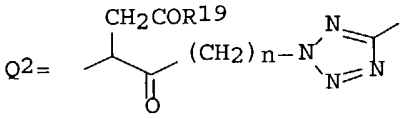
L9 ANSWER 5 OF 8 MARPAT COPYRIGHT 2004 ACS on STN
AN 129:302889 MARPAT Full-text
TI Preparation of tetrazole-containing peptide analogs as inhibitors of interleukin-1β converting enzyme
IN Omoto, Kazuayuki; Tanaka, Makoto; Miyazaki, Toru; Ono, Hiroyuki
PA Ono Pharmaceutical Co., Japan
SO Jpn. Kokai Tokkyo Koho, 31 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
FAN.CNT 1

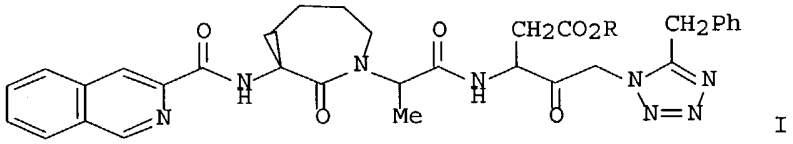
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI JP 10251295	A2	19980922	JP 1997-52183	19970307
PRAI JP 1997-52183	19970307			

GI







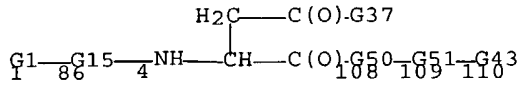


I

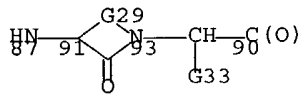
AB The title peptide analogs represented by formula R-AA1-AA2-NH-Y [R = H, R1-J-CO, R1-J-S(O)m; wherein J = single bond, C1-6 alkylene, C1-6 oxy-, amino, or thioalkylene, C2-6 alkenylene, carbocyclic or heterocyclic ring; R1 = C1-8 alkyl or alkoxy, C2-8 alkenyl or alkenyloxy, mono or di(C1-8 alkyl)amino, etc.; AA1 = single bond, NHCHR4CO; wherein R4 = H, (un)substituted C1-8 alkyl, (un)substituted carbocyclic or heterocyclic ring; AA2 = single bond, NR9CR10CO; wherein R9, R10 = H, (un)substituted C1-8 alkyl, (un)substituted carbocyclic or heterocyclic ring; or R9 and R10 are joined together to represent C1-6 alkylene or C2-6 alkenylene; or AA1 and AA2 are joined together to represent Q; wherein R15, R16 = H, C1-4 alkyl, Ph, (un)substituted phenyl-C1-4 alkyl; R17 = H, (un)substituted C1-8 alkyl, carbocyclic or heterocyclic ring; q = 2-12; one of C atoms in (CH2)q is replaced by O, S, SO, SO2, or (un)substituted NH or two adjacent H are removed to form a double bond; Y = Q1 or Q2; wherein R19 = C9-20 alkoxy, C3-7 cycloalkoxy, (un)substituted heterocyclyloxy, etc.; n = 1-4; Z = single bond, C1-6 alkylene, C2-6 alkenylene, O, S, CO, SO, SO2, (un)substituted NH, C1-6

alkylene with one of C atoms being replaced by O, S, SO, SO2, or (un)substituted NH; E = H, halo, CF3, diphenyl-C1-4 alkyl, tri(C1-4 alkyl)silyl, C1-4 alkyl, CO2H or its ester, (un)substituted CONH2 or NH2, etc.] are pr. These peptides are useful for the treatment of various inflammatory diseases. Thus, esterification of a peptide analog (I; R = H) with cyclobutylmethanol 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide and 4-dimethylaminopyridine in CH2Cl2 at room temperature for 12 h to give the title peptide I (R = cyclobutylmethyl), which showed more potent inhibitory activity (transferability into blood) against interleukin-1β converting enzyme than the free carboxylic acid I (R = H). A tablet formulation containing I (R = cyclobutylmethyl) was described.

MSTR 1



G2 = C(O)
G7 = alkylthio<(1-8)> (SO (-2) G14)
G13 = alkylene<(1-6)>
G15 = 87-1 90-4



G29 = CH2CH2CH2CH2
DER: or non-toxic salts or acid addition salts
MPL: claim 1
NTE: substitution is restricted

L9 ANSWER 6 OF 8 MARPAT COPYRIGHT 2004 ACS on STN
AN 128:308746 MARPAT Full-text
TI Preparation of peptides as selective factor Xa inhibitors
IN Zhu, Bing-Yan; Scarborough, Robert M.
PA COR Therapeutics, Inc., USA
SO PCT Int. Appl., 61 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9816523	A2	19980423	WO 1997-US18291	19971010
	WO 9816523	A3	19980618		
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	AU 9749809	A1	19980511	AU 1997-49809	19971010
	AU 720513	B2	20000601		
	EP 937073	A2	19990825	EP 1997-912697	19971010
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	JP 2001504810	T2	20010410	JP 1998-518454	19971010
	US 6262047	B1	20010717	US 1997-948672	19971010
PRAI	US 1996-33749P	19961011			
	US 1996-731366	19961011			
	US 1997-948672	19971010			
	WO 1997-US18291	19971010			

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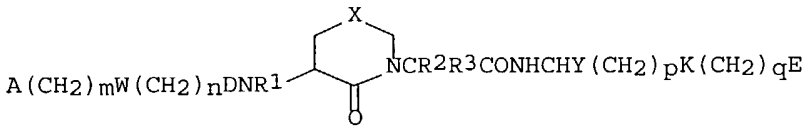

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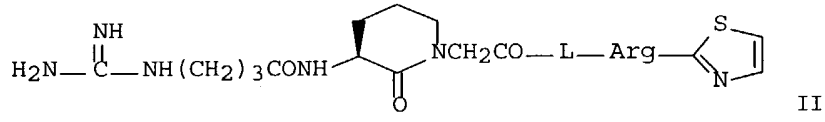
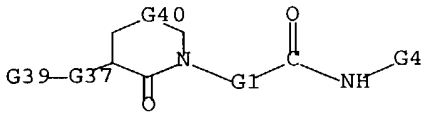


II

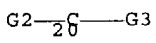
AB Heterocyclyl peptides I [R1 = H, alkyl, alkylaryl; R2 = H, alkyl, cycloalkyl, alkylaryl, alkylcycloalkyl, aryl; R3 = H, alkyl or R2 and R3 taken together form a carbocyclic ring; X = (CH2)q; m = 0-3, n = 0-6; p = 0-4; q = 0-2; A = heterocyclyl, H, OH, alkyl, aryl, alkylaryl,

(un)substituted NH2, NHC(:NH)NH2, C(:NH)NH2, NHCH:NH, CH:NH, or SC(:NH)NH2; W = direct link, alkyl, cycloalkyl, alkenyl, alkenylaryl, aryl, heterocyclyl; D = direct link, CO, SO2, CH2, OCO, (un)substituted NHSO2 or NHCO; K = direct link, cycloalkyl, aryl, heterocyclyl; E = H, OH, alkyl, aryl, alkylaryl, (un)substituted NH2, NHC(:NH)NH2, C(:NH)NH2, NHCH:NH, CH:NH, or SC(:NH)NH2; Y = H, B(OH)2 or ester, acyl group] having activity against mammalian factor Xa were prepared Thus, compound II was prepared for assay of antithrombotic efficacy.

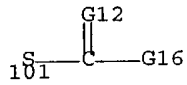
MSTR 1



G1 = 20



G17 = Ak<EC (1-) C, BD (0-) D (0) T> (SO (1-) G33)
G21 = 101

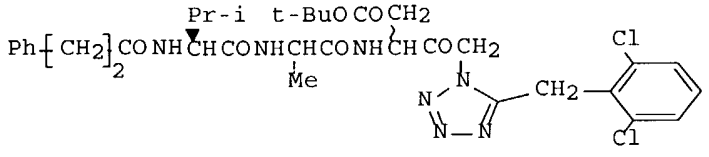


G36 = C(O)
G37 = NH
G40 = (0-2) CH2
MPL: claim 1
NTE: additional substitution and ring formation also claimed
STE: and optical isomers

L9 ANSWER 7 OF 8 MARPAT COPYRIGHT 2004 ACS on STN
AN 127:109196 MARPAT Full-text
TI Preparation of tetrazole moiety-containing peptides as interleukin 1β converting enzyme inhibitors
IN Ohmoto, Kazuyuki; Tanaka, Makoto; Miyazaki, Tohru; Ohno, Hiroyuki
PA Ono Pharmaceutical Co., Ltd., Japan; Ohmoto, Kazuyuki; Tanaka, Makoto; Miyazaki, Tohru; Ohno, Hiroyuki
SO PCT Int. Appl., 743 pp.
CODEN: PIXXD2
DT Patent
LA Japanese
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9724339	A1	19970710	WO 1996-JP3801	19961226
	W: JP, KR, US				
	RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	EP 889039	A1	19990107	EP 1996-942651	19961226
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	US 6136834	A	20001024	US 1998-101004	19980629
	US 6376484	B1	20020423	US 2000-572569	20000516
PRAI	JP 1995-351241	19951227			
	WO 1996-JP3801	19961226			
	US 1998-101004	19980629			

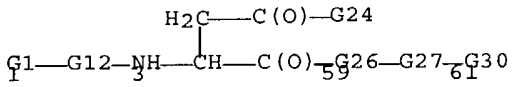
GI



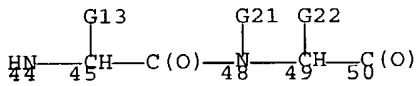
I

AB The title compds. R1COAA1AA2NHY [R1 represents H, alkyl, alkoxy, a carbocycle, a heterocycle, alkyl or alkoxy substituted by a carbocycle or a heterocycle, etc.; AA1 represents a single bond or NHCHR4CO; R4 = H, etc.; AA2 represents a single bond, etc.; further details on AA1 and AA2 are given; Y represents a group of formula CH[CH2CO2R19](CH2)nTetZE wherein Tet represents a tetrazole ring; Z represents alkylene, alkenylene, O, S, SO, SO2, etc.; E represents H, alkyl, etc.; R19 represents H, alkyl, etc.; n = 1 - 4] are prepared The title compound I in vitro showed IC50 of 0.03 μM against interleukin 1β converting enzyme.

MSTR 1



G2 = alkylene<(1-6)>
G5 = C(O)
G7 = S
G12 = 44-1 50-3

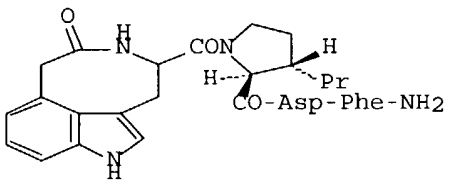


G23 = (2-12) CH2 (SO)
MPL: claim 1

L9 ANSWER 8 OF 8 MARPAT COPYRIGHT 2004 ACS on STN
AN 115:50308 MARPAT Full-text
TI Preparation of tetrapeptide type-B CCK receptor ligands
IN Chung, John Y. L.; Tufano, Michael D.; May, Paul D.; Shiosaki, Kazumi; Nadzan, Alex M.; Garvey, David S.; Shue, Youe Kong; Brodie, Mark S.; Holladay, Mark W.
PA Abbott Laboratories, USA
SO Eur. Pat. Appl., 101 pp.
CODEN: EPXXDW
DT Patent
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 405506	A1	19910102	EP 1990-112261	19900627
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
	CA 2020065	AA	19901231	CA 1990-2020065	19900628
	JP 03068597	A2	19910325	JP 1990-174287	19900630
PRAI	US 1989-375107	19890630			
	US 1990-531771	19900606			

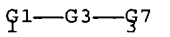
GI



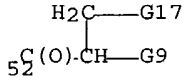
I

AB Type B-cholecystokinin (CCK) tetrapeptide agonists A-B-C-D [A = functionalized acetyl, RCO, R = heterotricyclic, carbotricyclic; B = functionalized aminopropionyl residue; A-B = functionalized piperazinedionyl, functionalized 5-amino-3-aza-4-oxohexanoyl; C = NR1CH(CH2R2)CO, R1 = H, lower alkyl, R2 = CO2H, tetrazolyl; B-C = bridged Ala-Asp residue or bridged tetrazolylalanine-Ala residue; D = functionalized ethylamino, functionalized tetrahydroisoquinolyl, functionalized piperazinon-1-yl, dehydrophenylalanine derivative; C-D = functionalized succinimidyl] and pharmaceutically acceptable salts thereof are prepared for treating a variety of disorders, including central nervous system disorders. Thus tetrapeptide I, prepared by solution coupling, possess affinity and selectivity for the cortical CCK receptor and stimulated calcium mobilization at CCK-B receptors on small cell lung cancer cell lines.

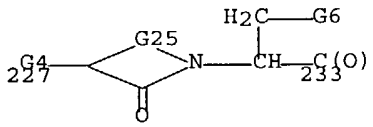
MSTR 1C



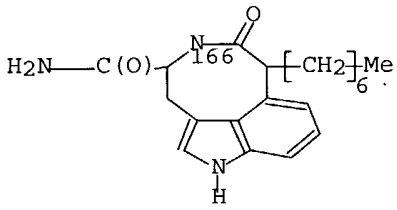
G1 = 52



G3 = 227-1 233-3



G4 = NH
G7 = 166



G9 = alkylthio<(1-7)>
G25 = (2-4) CH2
DER: or pharmaceutically acceptable salts
MPL: claim 1

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=> d l1; d his; log y
L1 HAS NO ANSWERS
L1                STR
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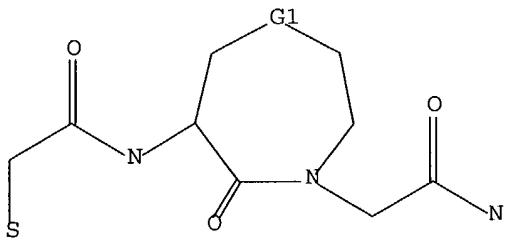

G1 C,N

Structure attributes must be viewed using STN Express query preparation.

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      FILE 'REGISTRY' ENTERED AT 18:36:54 ON 24 FEB 2004
L1                STRUCTURE UPLOADED
L2              1 S L1
L3             10 S L1 FUL

      FILE 'CAPLUS' ENTERED AT 18:37:19 ON 24 FEB 2004
L4              1 S L3

      FILE 'BEILSTEIN' ENTERED AT 18:37:49 ON 24 FEB 2004
L5              0 S L1
L6              0 S L1 FUL

      FILE 'MARPAT' ENTERED AT 18:38:04 ON 24 FEB 2004
L7              0 S L1
L8              9 S L1 FUL
L9              8 S L8 NOT L4
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COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	145.86	306.74

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-5.28	-5.97

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STN INTERNATIONAL LOGOFF AT 18:40:02 ON 24 FEB 2004
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